

II. REMARKS

Claims **56, 57, 59-67, 69, 70, 73-79 and 86-89** are pending in the subject application were examined and stand variously rejected. By this amendment and response, claims **67, 86 and 87** have been canceled without prejudice or disclaimer. Applicants respectfully reserve the right to file on or more continuation applications related to the same subject matter as the canceled claims.

Claims **56, 57, 62, 64, 65, 66, 76, 77, and 88** were amended. Many of the claims were amended to correct grammatical errors. The other amendments are supported in the specification. For example, support for the amendments to claims **56 and 57** is found in the application papers on page 34, lines 10 to 28. No new matter has been added by these amendments and entry thereof is respectfully requested.

In view of the preceding amendments and the remarks which follow, reconsideration and withdrawal of the rejections is respectfully requested.

Claim Informalities

Claims **62 and 64 to 67** stand objected to for alleged informalities. The claims have been amended in a sincere effort to remove the grounds for rejection. Reconsideration and withdrawal of the rejections is respectfully requested.

35 U.S.C. § 112, First Paragraph

Claims **56, 57, 59-67, 69, 73-79 and 86-89**, stand rejected under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter which was not describe in the specification in a manner to enable one of skill in the art to make and use the same.

Applicants respectfully traverse. With respect to claims **59-61, 63-67, 69, 73-79 and 89**, no specific stated grounds for rejection were alleged. For these reasons, the

rejection is improper and therefore should be removed against these claims.

With respect to the compounds of claim **62**, the Office alleged that they are directed to a vast number of chemical species that have not been described in the specification to enable the practitioner to make and use the same. The Office objected to the definition of substituents allegedly because the specification only supplies a limited number of examples.

Applicants respectfully traverse. The fact that the number of species encompassed is large as compared to the working examples in a specification is not, by itself, an adequate basis for rejection under 35 U.S.C. § 112, first paragraph. Applicants have not been provided technically specific statements of fact to which they can reply. For example, claim **62** presents two variables, the substituent of R1 and Q, and Q being limited to 5 specific structures with minor modifications. Which of the embodiments for R1 are beyond the scope of the specification? Which of the embodiments for Q (other than the phosphoramidate embodiment for R7 which is addressed) are beyond the scope of the specification, especially viewed in combination with the wealth of prior art, that Applicants have to the best of their ability, brought to the attention of the Patent Office? After the Examiner has provided a reasoned statement that specifically points out the alleged failures of the specification, Applicants can provide a rebuttal by submitting contrary evidence in the form of technical documents or declaration evidence. At this point Applicants would be guessing as to the technical basis for the rejections.

The Examiner also objected to claim **62** on the ground that "derivatives" or "analogues" in claim **62** is overly broad since structures are not provided. Applicants respectfully traverse. Claim **62** does not recite "analogues" and the derivatives are those which are "phosphoramidatyl derivatives of a naturally occurring amino acid". The term "derivative" is defined in Applicants' specification and is a term well known to those of skill in the art. Two specific derivatives are provided in the specification, leaving 18 possible derivatives remaining (there being 20 naturally occurring amino

acids). Applicants therefore request further clarification for the reasons provided above.

The Examiner also objected to the terms "stereoisomeric, enantiomeric and anomeric" in claim 62 on the ground that not all forms have been synthesized or that any reasonable predictive proportion of same have been tested to determine that the claimed pharmaceutical activity occurs in some subset thereof.

Applicants respectfully traverse. Applicants have provided the Office with a reasonable number of examples, not only by way of the subject specification but also by way of related applications that the Office has cited against the claims of this application. In addition, the Examiner has not provided any reason or technical basis for his assertion that one stereoisomeric form of the compound would be active while the other would not. Accordingly, it is difficult for Applicants to provide rebuttal evidence to overcome the basis for the rejection.

The Examiner also stated with respect to method claims 56, 57 and 86-88, the Examiner stated that the specification does not support the treatment of all diseases encompassed by the term cancer, autoimmune disorder and inflammatory conditions.

Applicants respectfully traverse. Applicants claims are not directed to the treatment of all cancers, autoimmune disorders and inflammatory conditions. Applicants' methods are directed only to those cells which overexpress thymidylate synthase, regardless of the type of cell. Colon cancer is only one such cancer cell.

Applicants' specification shows how to administer the compounds and the efficacy of the compounds. Whether one or other pathology is amenable to treatment by Applicants' methods can be determined by one of skill in the art, as expressed in Applicants' specification or alternatively, by published methods, for example those disclosed in US Patent Publication No.: US 2002/0039990 A1.

35 U.S.C. § 112, Second Paragraph

Claims **56-59, 61-63, 65, 72, 81-84 and 86-87** stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

With respect to claims **56 and 57**, the Examiner objected to use of the term “or a metabolite thereof formed after administration to the subject” because the particular structure is not defined. Applicants have amended claims **56 and 57** in a sincere effort to overcome the grounds for rejection.

The Office also objected to the use of the term “pathology characterized by hyperproliferative neoplastic cells” in claims **56, 57, 86 and 87** on the ground it is vague and indefinite. Applicants respectfully traverse on the ground that the claimed method is directed only to those various cells that overexpress thymidylate synthase, which has been linked to particular pathologies, without regard to specific cell type. Therefore, the claims are not as broad as the Examiner suggests. Removal of this ground for rejection is respectfully requested.

Claims **62, 86 and 87** stand rejected for the reasons of record. Applicants have amended the claims to overcome the stated grounds for rejection.

Double Patenting Rejections

The Office cited numerous grounds why the pending claims are unpatentable over Applicants' co-pending applications. Applicants respectfully defer responding to all double patenting rejections until allowable subject matter has been indicated by the Office in the subject application.

III. CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.


The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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